The formation of water in oil emulsion is necessary to prevent the encapsulated molecule from diffusing through the layer of oil phase surrounding the aqueous phase with the compound. The concentrated aqueous solution is emulsified, i.e. split into tiny droplets surrounded by layer of oil and subsequently a capsule is built around such droplets.

The water soluble, uncharged and small molecules can diffuse out from the capsule during the washing process due to concentration gradient that exists across-the capsule wall, i.e. high concentration inside and low concentration outside the capsule wall. Hence, the existing methods require formation of water in oil emulsion so that the molecule cannot diffuse through the layer of oil phase surrounding the aqueous phase with the compound. The concentration gradient is also a reason why, the concentration inside the capsule can never be higher than the concentration in the surrounding solution.

Hence, there is a need to provide an alternative method for encapsulation of small, uncharged and hydrophilic compounds. In particular, it is desired to provide a method of coupling or attaching such compounds with a reasonable loading efficiency and without altering the chemical and/or therapeutic properties of the compound. More particularly, it is desired to provide a method of encapsulating such compounds in a straightforward manner that obviates the need for using multi-phase emulsion systems.

Summary of Invention

According to one aspect of the present invention, there is provided a method of coupling an active compound to an ionomer complex, the method comprising at least one step selected from: (a) mixing a solution comprising at least one polycation and at least one polyanion, with the active compound; or (b) adding the polycation to a solution comprising the polyanion that is coupled to the active compound; or (c) adding the polyanion to a solution comprising the polycation that is coupled to the active compound; to thereby form the ionomer complex having the active compound encapsulated therein; wherein the active compound is uncharged and water soluble and of low molecular weight; wherein the interaction between said active compound and the ionomer complex is non-ionic and non-covalent in nature; wherein one of the polycation and polyanion is a block co-polymer comprising repeating neutral blocks and repeating charged blocks; and wherein the ratio of the neutral blocks to charged blocks in the block co-polymer is at least 3.

In another aspect, there is provided an ionomer complex comprising at least one active compound coupled thereto, wherein said active compound is uncharged and water-soluble, wherein the active compound is coupled to the ionomer complex via a non-ionic and non-covalent interaction**;** wherein said ionomer complex is formed from a reaction between a polycation and a polyanion, wherein at least one of the polycation or the polyanion comprises a block co-polymer, said block co-polymer comprising repeating neutral blocks and repeating charged blocks; and wherein the ratio of neutral blocks to charged blocks is at least 3.

It has been surprisingly found that the disclosed method is particularly useful for enclosing uncharged and water-soluble compounds. It has been further surprisingly found that the disclosed polyelectrolyte ionomer complexes are able to encapsulate these compounds in a stable manner, without requiring any ionic and/or covalent interactions between the compound being encapsulated and the ionomer complex. Advantageously, the present disclosure provides, for the first time, the ability to store, transport and deliver these small, uncharged compounds without altering their original chemical structures, functionalities and / or activities.

Further advantageously, the disclosed method provides a straightforward and spontaneous way of encapsulating the compound in a single mixing step, with substantial flexibility. For instance, the method may comprise mixing each of the polyanions, polycations and the active compound simultaneously. In other embodiments, the active compound may be first coupled to one of the polyions, prior to mixing with the oppositely charged polyion. It has been found that each of these disclosed embodiments result in the formation of an ionomer complex encapsulating one or more of these uncharged compounds.

Still advantageously, the disclosed method does not require the use of multiphase oil-in-water or water-in-oil emulsions; and thus does not require separate steps of removing the oil and recovering the active compound.

Definitions

The following words and terms used herein shall have the meaning indicated:

The term “uncharged”, when used herein to describe a compound or a molecule, means that the compound or molecule expresses no charges at all, whether positive or negative. In embodiments, this could mean that the compound or molecule comprises no charged ions or species. In another embodiment, an uncharged

Claims

1. A method of coupling an active compound to an ionomer complex, the method comprising at least one step selected from:

(a) mixing a solution comprising at least one polycation and at least one polyanion, with the active compound; or

(b) adding the polycation to a solution comprising the polyanion that is coupled to the active compound; or

(c) adding the polyanion to a solution comprising the polycation that is coupled to the active compound;

to thereby form the ionomer complex having the active compound encapsulated within therein;

wherein the active compound is uncharged and water soluble;

wherein the interaction between said active compound and the ionomer complex is non-ionic, and non-covalent in nature;

wherein one of the polycation and polyanion is a block co-polymer comprising repeating neutral blocks and repeating charged blocks; and

wherein the ratio of the neutral blocks to charged blocks in the block co-polymer is at least 3.

2. The method of claim 1, wherein the interaction is selected from the group consisting of: hydrogen bonding, hydrophobic interactions, Lenard-Jones interactions, and Van der Waals forces.

3. The method of claim 1, further comprising a step of selecting the polycation and the polyanion for forming the ionomer complex, such that the ionomer complex is capable of partaking in the non-ionic and / or non-covalent interactions with the active compound.

4. The method of claims 1-3, wherein said active compound has an atomic mass of less than 1 kDa.

5. The method of claim 1, wherein, in the block copolymer, the ratio of neutral blocks to charged blocks is about 5:1.

6. The method of any one of the preceding claims, wherein said ionomer complex comprises one or more functional groups selected from the group consisting of: an alcohol group, a carbonyl group, an ether group, an ester group, a carboxylic acid group, an amine group, an amide group, a carbamide group, an imine group, an imino group, an imidazole group, a guanidine group, a fluoro group and a cyano group, and wherein said one or more functional groups is coupled to the active compound by the non-ionic and non-covalent interaction.

7. The method of any one of the preceding claims, wherein the polyanion is selected from the group consisting of: polyacrylic acid, polymethacrylic acid, polystyrene sulfonate, polyphosphoric acid, polyglutamic acid and polyaspartic acid.

8. The method of any one of the preceding claims, wherein the polycation is selected from the group consisting of: poly-L-arginine, poly-D-arginine, poly-L-tryptophan, poly-D-tryptophan, poly-L-histidine, poly-D-histidine, α-poly-L-lysine, ε-poly-L-lysine, α-poly-D-lysine and ε-poly-D-lysine.

9. The method of claim 1, wherein said neutral block is selected from the group comprising polyethylene oxide (PEO), polytyrosine, polylactic acid, polycaprolactone, polyurethanes or polyanhydrides.

10. An ionomer complex comprising at least one active compound coupled thereto,

wherein said active compound is uncharged and water-soluble,

wherein the active compound is coupled to the ionomer complex via a non-ionic, and non-covalent interaction;

wherein said ionomer complex is formed from a reaction between a polycation and a polyanion, wherein at least one of the polycation or the polyanion comprises a block co-polymer, said block co-polymer comprising repeating neutral blocks and repeating charged blocks; and

wherein the ratio of neutral blocks to charged blocks is at least 3.

11. The ionomer complex of claim 10, wherein said active compound has an atomic mass of less than 1 kDa.

12. The ionomer complex of any one of claims 10-11, wherein, in the block co-polymer, the ratio of neutral blocks to charged blocks is about 5:1.

13. The ionomer complex of claim 10, wherein at least one of said polycation or polyanion or the ionomer complex comprises functional groups capable of coupling to the active compound via non-ionic and non-covalent interactions.

14. The ionomer complex of any one of claims 10-13, wherein each repeating group of the polyanion or of the polyanion comprises one or more functional groups selected from the group consisting of: an alcohol group, a carbonyl group, an ether group, an ester group, a carboxylic acid group, an amine group, an amide group, a carbamide group, an

imine group, an imino group, an imidazole group, a guanidine group, a fluoro group and a cyano group, said functional group being capable of coupling to said active compound via the non-ionic, and non-covalent interaction.

15. The ionomer complex of claims 10-14, wherein the polyanion is selected from the group comprising polyacrylic acid, polymethacrylic acid, polystyrene sulfonate, polyphosphoric acid, polyglutamic acid or polyaspartic acid.

16. The ionomer complex of claims 10-15, wherein the polycation is poly selected from the group comprising poly-L-arginine, poly-D-arginine, poly-L-tryptophan, poly-D-tryptophan, poly-L-histidine, poly-D-histidine, α-poly-L-lysine, ε-poly-L-lysine, α-poly-D-lysine or ε-poly-D-lysine.

17 The ionomer complex of claim 10, wherein said neutral block is selected from the group comprising polyethylene oxide (PEO), polytyrosine, polylactic acid, polycaprolactone, polyurethanes or polyanhydrides.